

**REMARKS**

Claims 1-3 and 5-13 are currently pending in the application, claim 1, 3 and 5-7 are withdrawn from consideration, and claims 2 and 8 have been amended. Support for the claim amendments may be found throughout the specification and claims as originally filed. In particular, support for the amendment to claim 2 may be found, for example, at page 28, lines 17-23. Support for the amendment to claim 8 may be found, for example, at page 20, lines 4-7, and page 17, lines 25-27. No new matter has been added.

Amendment of claims should in no way be construed as an acquiescence to any of the Examiner's rejections. The amendments to the claims are being made solely to expedite prosecution of the present application and do not, and are not intended to, narrow the claims in anyway. Applicants reserve the option to further prosecute the same or similar claims in the instant or in a subsequent patent application.

**Informalities**

Applicants note that they will correct the information in the specification and provide any appropriate statements regarding the ATCC deposit before payment of the issue fee for this application as required by 37 CFR §1.804. Applicants acknowledge that the Examiner will maintain the objection until such information has been submitted.

**Claim Objections**

Claim 8 was objected to for recitation of non-elected subject matter. Claim 8 has been amended and the amendment is believed to obviate the rejection. Accordingly, reconsideration and withdrawal of the objection is respectfully requested.

**Objection to New Matter added to Specification**

The office action alleges that the amendment filed June 2, 2003 introduces new matter into the specification because "[t]he specification does not indicate the nucleic acid sequence that hybridizes under stringent conditions to a nucleotide sequence of SEQ ID NO: 2 is at least 70% identical to the nucleotide sequence of SEQ ID NO: 2." Applicants respectfully disagree with the objection, however, in an effort to expedite prosecution of the application, Claim 2 has been amended. Support for the amendment to claim 2 may be found, for example, at page 28, lines

17-23. The amendment is believed to obviate the objection. Accordingly, reconsideration and withdrawal of the objection is respectfully requested.

**Rejection of Claims 2 and 8-12 Under 35 U.S.C. §112, first paragraph**

Claim 2 was rejected under 35 U.S.C. §112, first paragraph, for reasons of written description. In particular, the Action states that:

\*\*\*The specification indicates a nucleotide sequence which hybridizes under stringent conditions to a nucleic acid shown in SEQ ID NO: 2 or complement thereof can be used to isolate nucleic acids corresponding to 5' flanking regions of Csp genes from various animal species (page 32, lines 8-10, 19-20), but it does not indicate [that] the nucleic acid sequence is at least 70% identical to SEQ ID NO: 2. Moreover, the specification does not specify which portion of the nucleotide sequence is at least 70% identical to SEQ ID NO: 2. Without guidance on the nucleotide sequence that hybridizes under stringent conditions to SEQ ID NO: 2 and is 70% identical to SEQ ID NO: 2, one skilled in the art would not know how to identify this nucleic acid.\*\*\* (Office Action at 5)

The rejection is respectfully traversed.

Applicants note that claim 2 has been amended and the amendments are believed to obviate the rejection. In particular, claim 2 as amended is directed, at least in part, to nucleic acid sequences that hybridize under stringent conditions to a nucleotide sequence of SEQ ID NO: 2, wherein the nucleic acid sequence is at least 80% identical to the nucleotide sequence of SEQ ID NO: 2 over its entire length. Additionally, Applicants wish to point out that there are extensive teachings in the specification about how to identify nucleic acids that fall within the claim limitations. For example, stringent hybridization conditions are described in detail at page 31, line 17 to page 32, line 17 and percent identity is described at page 25, lines 4-20 and page 28, line 25 to page 29, line 5. At page 28, lines 17-23, the specification discloses that nucleic acids of the invention include those that are at least 80% identical to SEQ ID NO: 2. Therefore, based on the teachings in the specification, one of ordinary skill in the art would recognize that applicants were in possession of the claimed invention at the time of filing the application. Accordingly, reconsideration and withdrawal of the rejection is respectfully requested.

Claims 8-12 were rejected under 35 U.S.C. §112, first paragraph, for reasons of enablement. In particular, the Action states that "[t]he scope of the claims encompasses a method of identifying a compound that modulates the activity or level of a Csp protein, but the specification does not demonstrate monitoring the activity or the protein level of a Csp protein, and identifying the compounds as inhibitors or activators in the claimed method" (Office Action at 8). The rejection is respectfully traversed.

Applicants respectfully submit that to satisfy the enablement requirement the specification must contain “sufficient information regarding the subject matter of the claims as to enable one skilled in the art to make and use the claimed invention.” (MPEP §2164.01). Furthermore, “[t]he test for enablement is whether one reasonably skilled in the art could make or use the invention from the disclosures in the patent coupled with information known in the art without undue experimentation.” (*United States v. Teletronics, Inc.*, 8 USPQ2d 1217, 1223 (Fed. Cir. 1988); MPEP §2164).

Applicants respectfully submit that the specification provides sufficient guidance as to how to identify a compound that modulates the activity or level of a Csp protein. For example, the specification teaches a variety of methods to monitor the activity of a Csp protein, such as the ability to bind to calcineurin or inhibit calcineurin. The ability of a Csp protein to bind to a calcineurin protein may be determined, for example, using a two-hybrid screen as described at pages 123-125 and Figure 1. Alternatively, Csp-calcineurin interactions may be determined via immunoprecipitation as described at page 135, lines 16-26. Additionally, the ability of a Csp protein to inhibit calcineurin may be determined, for example, by assaying the effect of a Csp protein on the nuclear import of NF-AT, a process which requires calcineurin as described at page 125, line 25 to page 126, line 12, page 127, line 29 to page 128, line 16, and Figure 2. Alternatively, the inhibitory activity of a Csp protein on calcineurin may be determined by assaying a catalytic activity of calcineurin such as the ability of calcineurin to dephosphorylate the protein kinase A (PKA)-phosphorylated RII peptide substrate or to hydrolyze para-nitrophenyl phosphate (pNPP) as described at page 126, line 13 to 31, page 128, line 18 to page 129, line 2, and Figure 4. Furthermore, the specification teaches methods for monitoring the level of a Csp protein using antibodies (see e.g., page 133, line 23 to page 134, line 20 and Figure 23) or via a luciferase assay (see e.g., page 148, line 25 to page 149, line 3).

Additionally, the specification provides a working example of an assay used to identify an inhibitor of a Csp protein as described at page 129, line 20 to page 130, line 20 and Figure 16. In particular, Figure 16 shows that in the presence of calcium ionophores (I or iono) and phorbol 12-myristate 13-acetate (P or PMA) an elevated level of Csp was observed in human cells. However, treatment with cyclosporin A (CsA) was able to block the induction of Csp expression in cells exposed to ionophore and PMA. Further teachings about a variety of screening assays are provided at pages 103-105 of the specification.

As described above, the specification provides working examples, a variety of methods for assaying the level and activity of a Csp protein, and various teachings about screening assays to detect modulators of a Csp protein. Accordingly, the specification enables the skilled artisan to make and use the claimed invention without undue experimentation. Applicants respectfully

remind the Examiner that the Federal Circuit has sanctioned that “[e]nabling is not precluded even if some experimentation is necessary.” *Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 231 U.S.P.Q. 81 (Fed. Cir. 1986). Furthermore, the burden is on the Patent and Trademark Office to establish that experimentation would be undue, *In re Angstadt*, 190 U.S.P.Q. 214, 219 (C.C.P.A. 1976), taking into account the eight factors that are to be considered in determining whether a disclosure requires undue experimentation. *In re Wands*, 8 U.S.P.Q.2d 1400, 1404 (Fed. Cir. 1988). Applicants respectfully request that the Examiner withdraw the rejection.

**Rejection of Claims 8-13 Under 35 U.S.C. §112, second paragraph**

Claims 8-13 were rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite. In particular, the office action states that the term "activity of the Csp protein" renders the claim indefinite because "it is not clear what activity of the Csp protein is determined, and what the term "Csp" means." Claim 8 has been amended and the amendments are believed to obviate the rejection. Accordingly, reconsideration and withdrawal of the objection is respectfully requested.

Applicants believe that the claim amendments and remarks made herein fully address all issues raised in the Office Action. Silence with regard to any of the Examiner's rejections is not an acquiescence to such rejections. Specifically, silence with regard to Examiner's rejection of a dependent claim, when such claim depends from an independent claim that Applicant considers allowable for reasons provided herein, is not an acquiescence to such rejection of the dependent claim(s), but rather a recognition by Applicant that such previously lodged rejection is moot based on Applicant remarks and/or amendments relative to the independent claim (that Applicant considers allowable) from which the dependent claim(s) depends.

**CONCLUSION**

Applicants consider the Response herein to be fully responsive to the referenced Office Action. Based on the above Remarks, it is respectfully submitted that this application is in condition for allowance. Accordingly, allowance is requested. If a telephone conversation with Applicant's Attorney would expedite prosecution of the above-identified application, the Examiner is urged to call the undersigned at (617) 832-1000.

Respectfully submitted,

By:   
Jennifer K. Holmes, Ph.D.  
Reg. No. 46,778  
Agent for Applicants

Patent Group  
FOLEY HOAG LLP  
155 Seaport Blvd.  
Boston, MA 02210-2600  
Telephone: (617) 832-1000  
Facsimile: (617) 832-7000

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